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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/838,987	CHAMBERLAIN ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-16-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 10-21-04 have been fully considered but they are not persuasive.

The amendment filed 10-21-04 states claims 9-21 are canceled. However, claim 21 is still pending. Thus, only claims 9-20 have been canceled. Claim 23 has been added. Claims 1-8 and 21-23 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

In claim 5, the language remains wordy and confusing. Delete "encoding said antigen" for clarity. (It is readily apparent that the "nucleic acid inserts of the first and second recombinant vectors" refers to both the insert in the "first recombinant vector" of a) and in the "second recombinant vector" of b). The word "comprises" should be "comprise." The phrase "other than said antigen" should be --that is not said antigen— or --, wherein said immunostimulatory protein is not said antigen-- to clearly indicate the immunostimulatory protein is not the antigen.

Claim Rejections - 35 USC ' 112

The rejection of claims 1-8, 21 and 22 under 35 U.S.C. 112, first paragraph, because the specification, has been withdrawn. Wang of record taught using vectors encoding β-gal to protect mice against challenge with tumors expressing β-gal. Doolan (International J. Parasitology, 2001, Vol. 31, pg 753-762) taught DNA vaccines were

known to provide protection against malaria as of 1994 (pg 755, col. 2, Section 5). See also Sedegah (PNAS, October 1994, Vol. 91, pg 9866-9870). Thus, the amount of expression, route of administration and promoters required to obtain therapeutic/prophylactic levels of antigen expression were known in the art at the time of filing.

New claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrase "target antigen" in claim 23 is new matter because the phrase does not have support on pg 7, line 22, through pg 8, line 5, as asserted by applicants.

The phrase "CD8+ T cell epitopes of the target antigen" in claim 23 is new matter. The phrase does not have support on pg 7, line 22, through pg 8, line 5, as asserted by applicants, and none can be found in the specification as originally filed.

The phrase "a source of CD8+ T cell epitopes" in claim 23 is new matter. The phrase does not have support on pg 7, line 22, through pg 8, line 5, as asserted by applicants, and none can be found in the specification as originally filed. In particular, the specification is limited to administering vectors encoding antigens, which is much smaller in scope than claimed.

The compositions encompassed by steps i) and ii) of claim 23 are new matter. Steps i) and ii) appear to encompass administering compositions encoding an epitope

ut do not require the epitopes are the same. The specification is limited to dministering two vectors encoding the same antigen or epitope.

The phrase "non-replicating or replication impaired recombinant poxvirus vector" n claim 23 is new matter. The scope of vectors encompassed by the phrase was not resent in the specification as originally filed.

The phrase "with the proviso that if the source of epitopes in (i) is a viral vector, ne viral vector in (ii) is derived from a different virus" in claim 23 is new matter. The pecification does not contemplate that the vectors are different only with the ompositions being administered are viral vectors as claimed.

The rejection of claims 21 and 22 as under 35 U.S.C. 112, second paragraph, as eing indefinite for failing to particularly point out and distinctly claim the subject matter hich applicant regards as the invention has been withdrawn in view of the amendment.

Claim 5 as amended and new claim 23 are rejected under 35 U.S.C. 112, second aragraph, as being indefinite for failing to particularly point out and distinctly claim the ubject matter which applicant regards as the invention.

The phrase "said antigen against which an immune response is to be induced" in laim 5 lacks antecedent basis.

The phrase "target antigen" in claim 23 is indefinite. The metes and bounds of ntigens within the scope of the phrase cannot be determined and does not have an art-ecognized meaning.

The phrase "CD8+ T cell epitopes of the target antigen" in claim 23 is indefinite. The metes and bounds of epitopes within the scope of the phrase cannot be determined and does not have an art-recognized meaning.

The phrase "a source of CD8+ T cell epitopes" in claim 23 is indefinite. It is wholly unclear why the composition comprises a source of the epitopes and not the epitopes themselves. It is unclear if applicants intend the composition to comprise a source for the antigen such as a biotech company or catalog or if applicants intend the phrase to be limited to a composition comprising one or more CD8+ T cell epitopes. Deletion of "a source of" in steps i) and ii) is recommended. It is unclear whether the compositions are limited to vectors encoding the antigen or if the compositions encompass more than vectors encoding the antigens.

The structure of the compositions encompassed by steps i) and ii) of claim 23 are unclear. It is unclear whether the compositions are limited to vectors encoding the antigen or if the compositions encompass more than vectors encoding the antigens. Nowhere do steps i) and ii) require the epitopes are the same, which is the very nature of applicants invention. It is unclear if the phrase "including at least one CD8+ T cell epitope which is the same as a CD8+ T cell epitope of the priming composition" is intended to limit the epitope of the priming composition to the epitope of the boosting composition, or if the phrase is merely describing the source of the epitopes. Clarify the claim by deleting "one or more language" and using open claim language (which implies one or more), i.e. administering a priming vector encoding an antigen followed by administering a boosting vector encoding said antigen.

The phrase "wherein the source of CD8+ T cell epitopes is a non-replicating or replication impaired recombinant poxvirus vector in the mammal" makes claim 23 unclear. In particular, it makes the structure of the source of CD8+ T cell epitopes unclear. It is unclear if the phrase applies to only the boosting composition or if it applies to the priming composition and the boosting composition. It is unclear if the phrase is intended to encompass administering a vector encoding the antigen twice (once as a primer and once as a boost) or if the claim is limited to injecting different vectors encoding the same antigen. If the priming and boosting compositions are poxviruses, clearly set forth the structures as a composition comprising a poxvirus.

The phrase "with the proviso that if the source of epitopes in (i) is a viral vector, the viral vector in (ii) is derived from a different virus" is unclear. If the priming vector is not a viral vector, can the boosting vector be the same as the priming vector? It is unclear how the scope of "viral vector" in the phrase correlates to the scope of "poxvirus vector" also in the claim.

Claim Rejections - 35 USC ' 103

Claims 1-3 and 5-7 remain rejected and claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (May 1, 1995, J. Immunol., Vol. 154 (9) 4685-92) for reasons of record.

Wang taught administering a wild-type vaccinia virus (VV) to mice followed by administering a fowlpox virus (FPV) encoding β-gal which caused an increase in CTL response in splenocytes as compared to administering wild-type vaccinia followed by

vaccinia encoding β-gal (pg 4689, col. 2, Fig. 6, 1st full ¶). The increased CTL response is "an immune response" against the "at least one antigen" as claimed. Wang did not teach administering VV-β-gal followed by administering FPV-β-gal. However, Wang taught a vaccinia VV-β-gal. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer VV-β-gal followed by FPV-β-gal as taught by Wang. One of ordinary skill in the art at the time the invention was made would have been motivated to replace wild-type VV with VV-β-gal to introduce the DNA encoding β-gal sooner thereby inducing the immune response sooner.

Similarly, Wang taught administering a wild-type FPV followed by VV-β-gal, which also caused an immune response (page 4689, col. 2, 1st ¶). Wang did not teach administering FPV-β-gal followed by VV-β-gal. However, Wang taught administering FPV-β-gal caused an immune response. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer FPV-β-gal followed by VV-β-gal. One of ordinary skill in the art at the time the invention was made to replace wild-type FPV with FPV-β-gal to introduce the DNA encoding β-gal sooner and induce the immune response sooner. Claim 5 is included because VV and FPV encode viral proteins that are recognized as foreign and induce an immune response.

Claim 23 is included because it is so unclear (see 112/2nd).

Applicants argue Wang does not teach administering two different vectors encoding the same antigen. Applicants argue motivation to replace the wild-type VV with VV-β-gal cannot be found in Wang. Applicants' arguments are not persuasive.

Wang does not have to explicitly suggest replacing the wild-type VV with VV-β-gal for motivation to replace the wild-type VV with VV-β-gal to exist.

The examiner has established that Wang represents the knowledge of one of ordinary skill in the art at the time of filing. Wang taught using both VV-β-gal and FPV-β-gal *in vivo*. Wang taught interchanging FPV and VV vectors. Wang also provides evidence that the knowledge of one of ordinary skill in the art at the time of filing included the desire to induce a CTL response in tumors as soon as possible *in vivo* using combinations of FPV and VV vectors to prevent death (see for example Fig. 5). Wang taught administering a wild-type FPV followed by VV-β-gal. Therefore, Wang taught administering two different vectors. Wang taught administering FPV-β-gal followed by FPV-β-gal (Fig. 5C). Therefore, Wang taught administering FPV-β-gal first followed by a second vector encoding β-gal, i.e. pre-immunization with FPV-β-gal. Thus, combining the experiments described by Wang would easily lead of one of ordinary skill in the art to administering VV-β-gal followed by FPV-β-gal. The motivational statements provided by the examiner represent the knowledge of one of ordinary skill in the art at the time of filing, which is readily apparent from the teachings of Wang.

Applicants argue Wang does not relate to a prime-boost regimen, as is the instant application. Applicants' argument is not persuasive because the claims are not limited to a "prime-boost" regimen. Please correlate arguments to the claims. Furthermore, Wang does relate to a "prime-boost" regimen because the purpose was to

enhance the immunogenicity of tumor cells expressing β-gal using two different vectors (abstract; pg 4690, last ¶). Pg 4689, col. 2, specifically refers to "preimmunization" with rVV, which is equivalent to priming the immune system as argued. Applicants argue no benefit is demonstrated by preimmunization with rVV. Applicants' argument is not persuasive because the claims simply require inducing an immune response against the antigen. The claims do not require improving the immune response as compared to administering FPV-β-gal alone.

Applicants argue Fig. 1C of the instant application shows unexpected results as compared to Fig. 5C of Wang. Applicants' argument is not persuasive. The two figures cannot be compared to establish unexpected results. Fig. 1C of the instant application describes the survival of mice injected with wild-type FPV followed by VV-β-gal (VJS6) (pg 21, lines 26-35). Fig. 5 of Wang describes the survival of mice injected with FPV-lacZ twice. A proper comparison to Fig. 5C of Wang would replace the first FPV-lacZ injection of Wang with VV-lacZ. Injecting VV-lacZ followed by FPV-lacZ and obtaining an increased survival beyond Fig 5C would be evidence of an unexpected result. Applicants could also provide evidence that administering rVV-β-gal followed by FPV-β-gal had better results than administering wild-type rVV followed by FPV-β-gal explicitly described in the "VV/FPV" of Fig. 6 on pg 4689 of Wang (col. 2, "Preimmunization...").

Claims 1-3, 5-7, 21 and 22 remain rejected and claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (May 1, 1995, J. Immunol., Vol. 154 (9) 4685-92) for reasons of record.

Wang taught administering VV-β-gal to mice followed by FPV-β-gal or vice versa, which caused an immune response (see 103 rejection above). Wang did not expressly teach replacing β-gal with MART-1 or gp100. However, Wang suggested replacing β-gal with MART-1 and gp100 and taught making FPV-MART-1 and FPV-gp100 (pg 4690, col. 2, last 2 ¶). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Wang wherein the β-gal gene is replaced with MART-1 or gp100 as suggested by Wang. One of ordinary skill in the art at the time the invention was made would have been motivated to replace β-gal with MART-1 or gp100 to determine if self proteins such as MART-1 or gp100 induced the same immune response as β-gal and to determine if MART-1 or gp100 enhanced the precursor frequency of T-cells that recognize MART-1 or gp100 prior to *ex vivo* expansion (pg 4690, col. 2, ¶ 2, line 4).

Claim 23 is included because it is so unclear (see 112/2nd).

Applicants have not addressed this rejection. Applicants are reminded that to be fully responsive, each rejection must be argued separately. The arguments may be repeated and the arguments for the second obviousness may refer to arguments made in the first obviousness rejection; however, applicants cannot argue two rejections together.

Claim 1-8 remain rejected and claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (J. Immunol., (1995 May 1) 154 (9) 4685-92) in view of Zhai (Jan. 15, 1996, J. Immunol., Vol. 156, No. 2, pages 700-710) for reasons of record.

Wang taught administering VV-β-gal to mice followed by FPV-β-gal, which caused an increase in CTL response in splenocytes as compared to administering two doses of vaccinia virus encoding β-gal. Wang did not teach replacing the vaccinia virus or fowlpox virus with an adenovirus. However, Zhai taught administering an adenoviral vector encoding β-gal to mice and obtaining an immune response.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Wang wherein the vaccinia virus or fowlpox virus was replaced with the adenoviral vector taught by Zhai. One of ordinary skill in the art at the time the invention was made would have been motivated to replace the vaccinia virus (the first vector) with the adenoviral vector to increase the CTL response against antigen as compared to administering adenoviral vector followed by readministration of adenoviral vector. One of ordinary skill in the art at the time the invention was made would have been motivated to replace the fowlpox virus (the second vector) with the adenoviral vector to determine if fowlpox was the only virus that could be used to obtain a CTL response against antigen after administering vaccinia virus.

Claim 23 is included because it is so unclear (see 112/2nd).

Applicants argue the claims are not obvious in view of Wang for reasons above and Zhai does not cure the deficiencies of Wang. Applicants mention the deficiencies of Zhai but do not provide any specific arguments regarding why the combined teachings of Wang and Zhai do not teach all the limitations of the claims or why motivation is lacking (pg 8 of response). Applicants' argument is not persuasive. The combined

teachings of Wang and Zhai taught all the limitations of claim and one of ordinary skill in the art would have been motivated to combine the teachings of Wang and Zhai. Applicants have not pointed to one limitation that is missing from the references or why motivation to combine the references would be lacking.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the

office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER